944 Electrophysiology — Basic and Ventricular Arrhythmias

Tuesday, March 21, 1995, 9:00 a.m.–11:00 a.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: 10:00 a.m.–11:00 a.m.

944-68 A Comparison Between the Pro-Arrhythmic Effect of Almokalant and d-Sotalol in an Animal Model of Torsade de Pointes Arrhythmias

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Administration of class III agents may promote the development of Torsade de Pointes arrhythmias (TdP). We have developed a chronic AV block dog model in which after d-sotalol (dS) TdP can be reproducibly induced by pacing. The response is also reproducible over weeks. In this model of TdP we compared the proarrhythmic effect of d-sotalol (2 mg/kg) and Almokalant (A, 0.12 mg/kg) in the same dog. In 7 anesthetized dogs with chronic AV block (4 ± 2 wks) dS was administered, and A in a second experiment (4 ± 1.6 wks later). In 5/7 dogs monophasic action potentials were endocardially recorded in the right and in the left ventricle (RV, LV) to register EADs and to measure the action potential duration (APD). Dispersion of repolarization (ΔAPD) was defined as LV APD — RV APD.

Results. Baseline conditions were identical in the two experiments in the same dog (cycle length of the idioventricular rhythm, CL-IVR:1620 ± 335 ms, QT:405 ± 50 ms, LV APD:385 ± 40 ms, RVAPD:340 ± 32 ms, ΔAPD: 45 ± 25 ms). The CL-IVR and QT time increased with resp. 20 and 27% after dS and with 20 and 34% after A. EADs were more frequently observed after A (5/5) than after dS (3/5). Induction of TdP was more frequently seen after A: spontaneous TdP was observed in 4/7 dogs, the incidence increased to 5/7 after pacing. After dS TdP was only induced by pacing (2/7). Induction was found to be related to ΔAPD. After both drugs the LV APD increased more than the RV APD. LV APD after A (575 ms) was also longer than QT time (550 ms). The ΔAPD increased more after A than dS (40 ± 18 to 125 ± 95 ms vs 45 ± 30 to 85 ± 70 ms, $P < 0.05$).

Conclusions. A induced more EADs and led to a larger ΔAPD than dS in the same dog. These changes were related to a higher incidence of TdP. The findings show the value of our model to evaluate TdP induction by different drugs.

944-69 Anisotropic Repolarization in Ventricular Tissue

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In the *in vivo* preparation, the effective refractory period (ERP) of epicardial ventricular cells is significantly influenced by the sequence of activation. Previous *in vitro* studies, however, showed the effects of myocardial fiber orientation (MFO) on ERP were only apparent within 2–3 mm from the site of baseline stimulation (S_1). To determine the importance of the MFO on the repolarization process, we studied 12 blocks of pig RV tissue in vitro. The size of each block was 30 mm × 30 mm × 2 mm. Transmembrane action potentials (APs) were recorded and ERP were measured from the epicardial surface which has nearly uniform MFO. The tissue was paced at a 500 ms cycle length, and sequential recordings were made at 1, 4, 7, 10, 13, and 16 mm from S_1 along and across the fibers. *Results:* The propagation of depolarization was slower ($p < 0.01$) in the transverse (0.18 m/s) than in the longitudinal direction (0.34 m/s). In the transverse direction, AP duration 1 mm away from the S_1 site was 188 ± 14 ms, and progressively shortened as the recording site was moved further away from the S_1 site ($p < 0.001$). In contrast, the AP duration in the longitudinal direction did not change as the distance between recording site and the S_1 site increased. The ERP 16 mm from the site of stimulation was longer in the transverse direction (280 ± 19 ms) than in the longitudinal direction (252 ± 12 ms, $p < 0.01$), but the difference was less than that between activation times, reflecting opposite effects of MFO on activation and repolarization. *Conclusion:* The effects of MFO on repolarization was apparent only when propagation was across the fiber. The effects of MFO are present at sites ≥16 mm from the S_1, and could explain the results of *in vivo* studies.

944-70 Effects of Graded Intracoronary Infusion of Heptanol on Conduction and Susceptibility to Inducible Arrhythmias in Infarcted Canine Myocardium In Vivo

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Abnormal intracellular coupling is an important element of the arrhythmia substrate in chronic coronary artery disease. To determine the effects of changing cellular coupling on epicardial conduction and susceptibility to inducible ventricular tachycardia (VT), graded intracoronary infusion of heptanol (H) was performed in 9 dogs with chronic (6–18 weeks) occlusion-reperfusion LAD infarction. The LAD was supplied with blood via a constant flow bypass system, allowing selective infusion of known, fixed concentrations of H. Activation time (AT) during sinus rhythm (NSR) was measured at 40 epicardial sites in a 0.5 × 1.0 cm plaque positioned within the field of the LAD bypass system. Programmed stimulation (up to three extrastimuli) was performed at each H concentration. *Results:*

	Control	H (0.5 mM)	H (1.0 mM)
Number of dogs	9	9	7
AT (change vs control)	–	108%	151%
Noninducible	8	4	3
Sustained VT	0	4	1
Sustained PMVT/VF	1	1	3

VT was induced in one dog at 1.0 mM H despite the absence of electrical activity in the perfusion field during NSR. *Conclusions:* 1) low dose H (0.5 mM) increases susceptibility to inducible VT; 2) high dose H (1.0 mM) decreases susceptibility to inducible VT with significant decreases in conduction or conduction block during NSR; and 3) VT may be induced in this model despite the absence of electrical activity in the LAD perfusion field. This suggests that the border zone between normal and H perfused tissue may contribute to arrhythmogenesis. These observations support the hypothesis that the antiarrhythmic effect of uncoupling agents may be mediated by dissociating poorly coupled cells in infarcted myocardium.

944-116 Focal Activation Patterns of Cesium Chloride Induced Torsades-de Pointes Tachycardias

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"Torsades-de-pointes" tachycardias are probably initiated by early after depolarizations causing triggered activity. Whether successive beats with their constantly changing amplitude and axis result from focal or reentrant mechanisms has not yet been elucidated. Three dimensional mapping was carried out in 4 beagle dogs with polymorphic ventricular tachycardia (PVT) induced by repetitive (every 10 minutes) doses of cesium chloride (CsCl, 1 mmol/kg i.v.). Bradycardia was produced by radiofrequency ablation of the AV node. Bipolar left and right ventricular electrograms were simultaneously recorded from 240 endo-, epi- and intramyocardial sites through 60 pins containing 4 bipolar electrodes each (interelectrode distance 2 mm, distance between pins 10–15 mm). One (3 dogs) or two (1 dog) doses of CsCl produced various episodes of PVT, nine of which were analyzed (6.8 ± 2.7 consecutive beats). PVT originated from various left (n = 3) or right (n = 6) ventricular endocardial sites. Slow conduction or conduction block was not evident, total ventricular activation time during consecutive beats was 75 ± 12 msec. Initiation and continuation of PVT appeared to be exclusively due to focal mechanisms. Three different activation patterns were observed: (1) Changing foci from beat to beat, with variable coupling intervals (n = 2); (2) Two competing endocardial foci firing at variable rates (n = 3); (3) Periodically changing foci, replacing each other after gradual slowing of respective intrinsic rates (n = 4).

Conclusions: Compatible with triggered activity elicited in Purkinje fibers, CsCl induced PVT demonstrate a focal activation pattern with an endocardial site of earliest activation. Local foci may initially speed up and then slow down in rate. Competing foci apparently rather trigger than suppress activation of each other.

944-117 The Effect of Pacing Site on the Upper Limit of Ventricular Vulnerability

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The critical point hypothesis for the upper limit of ventricular vulnerability (ULV) predicts that the activation sequence should not affect the ULV shock strength. Conversely, it predicts that for shocks slightly weaker than the ULV, the time within the T-wave at which VF is induced should change with the activation sequence. Thus, the purpose of this study was to determine the